=> file casreact
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FILE CONTENT:1840 - 11 Dec 2005 VOL 143 ISS 24

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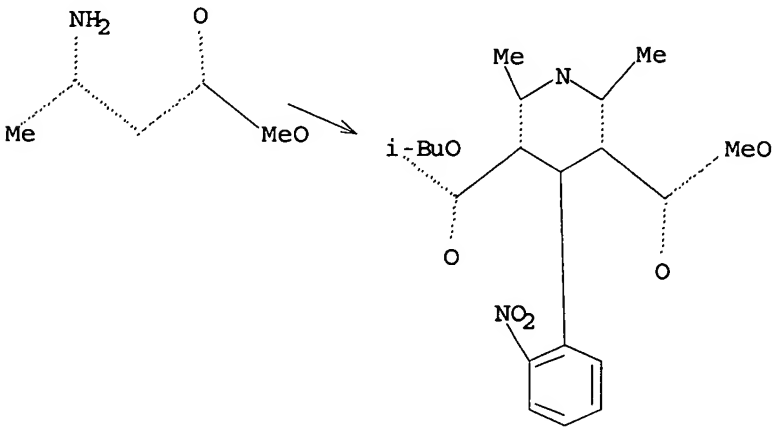
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que
L1 STR



Structure attributes must be viewed using STN Express query preparation.
L3 3 SEA FILE=CASREACT SSS FUL L1 (9 REACTIONS)

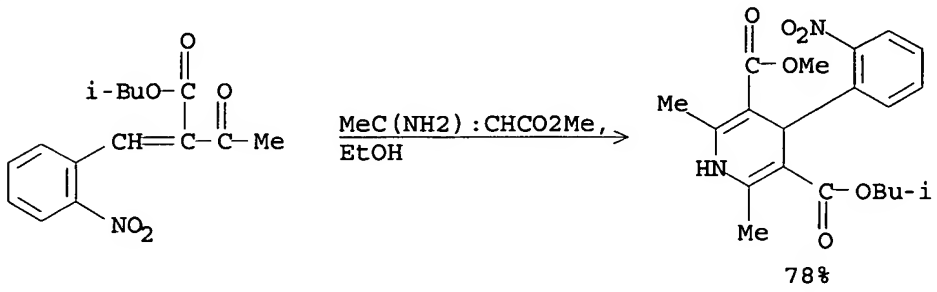
=> d l3 1-3 ibib abs fcrd

L3 ANSWER 1 OF 3 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 143:367186 CASREACT
TITLE: Study on synthesis of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxlic acid isobutyl methyl ester
AUTHOR(S): Chen, Yaping; Yu, Bin
CORPORATE SOURCE: Department of Chemical Technology, Jiang Yin Vocational College, Jiangyin, 214433, Peop. Rep. China
SOURCE: Wuxi Qinggong Daxue Xuebao (2003), 22(4), 57-59, 68

CODEN: WQDXF3; ISSN: 1009-038X
PUBLISHER: Wuxi Qinggong Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB An improved three-steps method for synthesis of 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxlic acid iso-Bu Me ester with anti-hypertension activity was reported. The process has the advantage of short reaction time, and improved yield. The structure of the final product was confirmed by elemental anal., IR, 1H NMR and 13C NMR.

RX(3) OF 6



CON: room temperature -> reflux

L3 ANSWER 2 OF 3 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:77036 CASREACT
TITLE: Industrial production process for the synthesis of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (nisoldipine)
INVENTOR(S): Ferrari, Massimo; Ghezzi, Marcello; Alberelli, Manuel; Ambrosini, Alberto
PATENT ASSIGNEE(S): Erregierre S.p.A., Italy
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

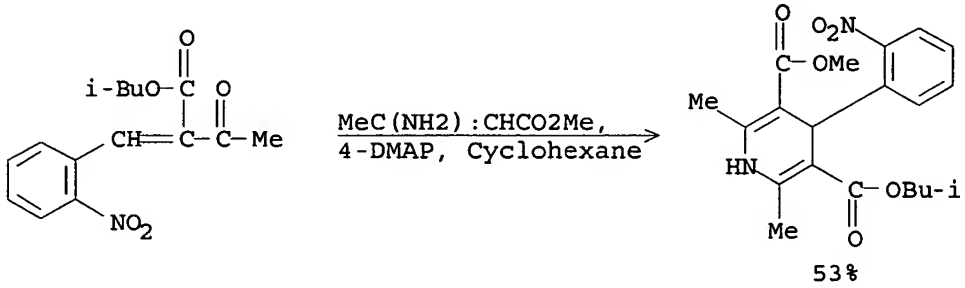
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002958	A1	20040108	WO 2003-EP6755	20030626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1532110	A1	20050525	EP 2003-761517	20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005240022	A1	20051027	US 2005-520066	20050103

PRIORITY APPLN. INFO.: IT 2002-MI1445 20020701
WO 2003-EP6755 20030626

AB The process of iso-Bu Me 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (Nisoldipine) synthesis is by the reaction of

iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate in an apolar solvent, added to the reaction mixture in a single portion or portionwise in an apolar solvent, to give crude Nisoldipine, purified by crystallization from a water/water soluble solvent mixture such as water/acetone mixture

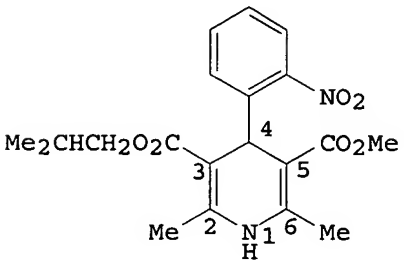
RX(2) OF 3



NOTE: work up
CON: STAGE(1) 10 hours, reflux; 16 hours, reflux

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

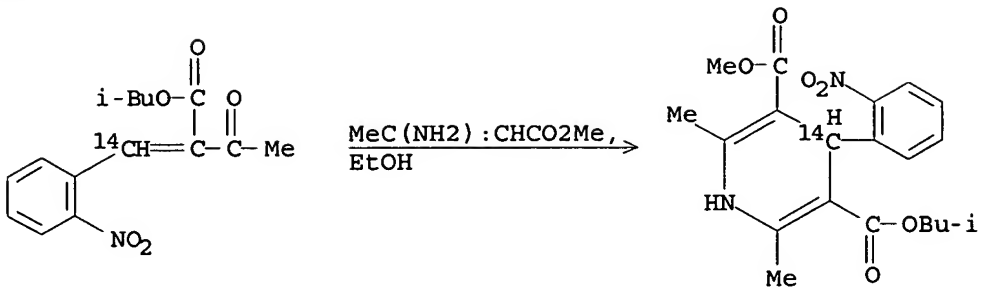
L3 ANSWER 3 OF 3 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 112:138871 CASREACT
TITLE: Syntheses of [4-carbon-14]- and [6-carbon-14]nisoldipine
AUTHOR(S): Scherling, D.; Pleiss, U.
CORPORATE SOURCE: Inst. Pharmacokinet., Bayer A.-G., Wuppertal, D-5600, Fed. Rep. Ger.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(12), 1393-400
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The synthesis of [4-14C]nisoldipine I starting from di-Me [14C]formamide (II) was described. II reacts with 2-O2NC6H4Li yielding 2-nitro[7-14C]benzaldehyde which on Knoevenagel condensation with iso-Bu acetoacetate yielded iso-Bu 2-(2-nitro[7-14C]benzylidene)acetoacetate (III). Key reaction step was the cyclizing Michael addition III with Me 3-aminocrotonate to give I.

RX(3) OF 27



NOTE: In dark

=> => file caplus
FILE 'CAPLUS' ENTERED AT 09:49:06 ON 13 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 13 Dec 2005 VOL 143 ISS 25
FILE LAST UPDATED: 12 Dec 2005 (20051212/ED)

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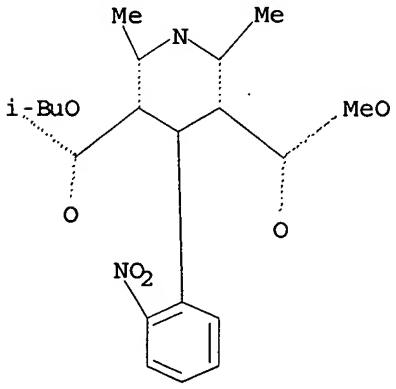
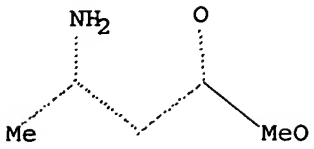
http://www.cas.org/infopolicy.html

=> d que
L4 STR



Structure attributes must be viewed using STN Express query preparation.

L5 STR



Structure attributes must be viewed using STN Express query preparation.
L6 21 SEA FILE=REGISTRY SSS FUL L4
L7 315 SEA FILE=REGISTRY SSS FUL L5
L9 11 SEA FILE=CAPLUS L6 AND L7

=> d l9 1-11 ibib abs hit

L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1065302 CAPLUS
DOCUMENT NUMBER: 143:367186
TITLE: Study on synthesis of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxlic acid isobutyl methyl ester
AUTHOR(S): Chen, Yaping; Yu, Bin
CORPORATE SOURCE: Department of Chemical Technology, Jiang Yin Vocational College, Jiangyin, 214433, Peop. Rep. China
SOURCE: Wuxi Qinggong Daxue Xuebao (2003), 22(4), 57-59, 68
CODEN: WQDXF3; ISSN: 1009-038X
PUBLISHER: Wuxi Qinggong Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 143:367186
AB An improved three-steps method for synthesis of 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxlic acid iso-Bu Me ester with anti-hypertension activity was reported. The process has the advantage of short reaction time, and improved yield. The structure of the final product was confirmed by elemental anal., IR, 1H NMR and 13C NMR.
IT **14205-39-1P** **61312-59-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of dihydrodimethyl(nitrophenyl)-pyridinedicarboxlic acid iso-Bu Me ester)
IT **63675-72-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of dihydrodimethyl(nitrophenyl)-pyridinedicarboxlic acid iso-Bu Me ester)

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20659 CAPLUS
DOCUMENT NUMBER: 140:77036
TITLE: Industrial production process for the synthesis of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (nisoldipine)
INVENTOR(S): Ferrari, Massimo; Ghezzi, Marcello; Alberelli, Manuel; Ambrosini, Alberto
PATENT ASSIGNEE(S): Erregierre S.p.A., Italy
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002958	A1	20040108	WO 2003-EP6755	20030626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1532110	A1	20050525	EP 2003-761517	20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005240022	A1	20051027	US 2005-520066	20050103
PRIORITY APPLN. INFO.:			IT 2002-MI1445	A 20020701
			WO 2003-EP6755	W 20030626

OTHER SOURCE(S): CASREACT 140:77036

AB The process of iso-Bu Me 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (Nisoldipine) synthesis is by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate in an apolar solvent, added to the reaction mixture in a single portion or portionwise in an apolar solvent, to give crude Nisoldipine, purified by crystallization from a water/water soluble solvent mixture such as water/acetone mixture

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

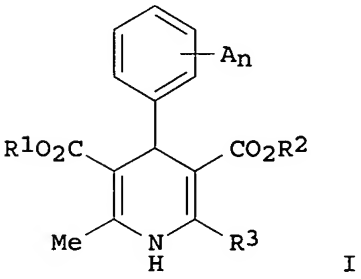
IT 552-89-6, 2-Nitrobenzaldehyde 7779-75-1, Isobutyl acetoacetate
14205-39-1, Methyl 3-aminocrotonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of nisoldipine by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)

IT **63675-72-9P**, Nisoldipine
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)

L9 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:573777 CAPLUS
DOCUMENT NUMBER: 133:177100
TITLE: Preparation of unsymmetrical 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates.
INVENTOR(S): Bozsing, Daniel; Kovanyine Lax, Gyorgyi; Simig, Gyula; Tompe, Peter; Blasko, Gabor
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047560	A2	20000817	WO 2000-HU12	20000215
WO 2000047560	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: HU 1999-353 A 19990215
OTHER SOURCE(S): CASREACT 133:177100; MARPAT 133:177100
GI



I

AB Title compds. (I; R1, R2 = alkyl, methoxyethyl, cyanoethyl; R1 and R2 are different; R3 = alkyl, hydroxyalkyl, haloalkyl, PhCH2OCH2, CH2OCH2CH2X; X = halo, N3, NR4R5; R4, R5 = H, alkyl; R4R5N = phthaloyl; A = NO2, halo; n = 1, 2) were prepared by (a) reaction of (II; A, n as above) with R1O2CH2COMe and R2O2CCH:C(NH2)R3 (R1-R3 as above); or (b) reaction of II with R2O2CH2COR3 and R1O2CH:C(NH2)Me (R1-R3 as above) and if desired further transformations of I into other I. Thus, 1-(3-nitrophenyl)-N,N'-bis(3-nitrobenzylidene)methylenediamine, Me 3-aminocrotonate, and Et acetoacetate were refluxed 15 h in isopropanol to give 86% 3-ethyl-5-methyl-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (nitrendipin).

IT **63675-72-9P** 79781-21-8P 88150-62-3P 107812-86-2P 221446-45-3P 288254-53-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of asym. 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates)

IT 105-45-3, Methyl acetoacetate 141-97-9, Ethyl acetoacetate 638-07-3, Ethyl 4-chloroacetoacetate 1498-93-7 6334-18-5, 2,3-Dichlorobenzaldehyde 7318-00-5, Ethyl 3-aminocrotonate **14205-39-1**, Methyl 3-aminocrotonate 39562-70-4 51625-68-4 67354-34-1, Ethyl 4-benzyloxyacetoacetate 85518-49-6, Ethyl 4-hydroxyacetoacetate 88150-75-8 126192-88-9 130000-32-7, 2-Methylpropyl acetoacetate 288254-56-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of asym. 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates)

L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:271337 CAPLUS
DOCUMENT NUMBER: 130:296614
TITLE: Pyridyl compounds and pharmaceutical compositions containing them
INVENTOR(S): Statkow, Pierre; Straumann, Danielle; Chatterjee, Shyam S.; Sunkel Letelier, Carlos; Fau De Casa-Juana

Munoz, Miguel; Alvarez-Builla, Gomez Julio; Minguez Ortega, Jose M.
PATENT ASSIGNEE(S): Cermol S.A., Switz.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919302	A1	19990422	WO 1998-IB1555	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CH 692199	A	20020315	CH 1997-2364	19971009
CH 692199	A8	20020614		
CA 2306789	AA	19990422	CA 1998-2306789	19981007
AU 9892771	A1	19990503	AU 1998-92771	19981007
AU 747150	B2	20020509		
EP 1023267	A1	20000802	EP 1998-945453	19981007
EP 1023267	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001519415	T2	20011023	JP 2000-515875	19981007
AT 250034	E	20031015	AT 1998-945453	19981007
PT 1023267	T	20040130	PT 1998-945453	19981007
ES 2206989	T3	20040516	ES 1998-945453	19981007
US 6482841	B1	20021119	US 2000-529112	20000407

PRIORITY APPLN. INFO.: CH 1997-2364 A 19971009
WO 1998-IB1555 W 19981007

OTHER SOURCE(S): MARPAT 130:296614

AB The present invention is concerned with new pyridine double esters, their acids, and pharmaceutically acceptable salts. These compds. can be obtained by oxidation of the corresponding 1,4-dihydropyridines, and they are useful as cardioprotective agents in pharmaceutical compns. 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-phenyl-1,4-dihyropyridine-3,5-dicarboxylate, prepared in 82% yield from Me benzylideneacetoacetate and 2-tetrahydrofuranylmethyl 3-aminocrotonate, was oxidized to give 59% 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylate. Approx. 30 other title compds. were similarly prepared 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate, prepared in 79% yield by oxidation of its 1,4-dihydro analog, gave 100% protection against death and ventricular fibrillation in rats in which coronary occlusion and reperfusion were induced.

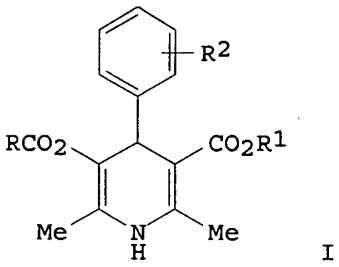
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 85677-93-6 89267-41-4 **103026-83-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of cardioprotectant pyridine double esters)

IT 100-37-8, Diethylaminoethanol 105-45-3, Methyl acetoacetate 108-01-0, Dimethylaminoethanol 447-61-0, 2-Trifluoromethylbenzaldehyde 622-40-2, 4-(2-Hydroxyethyl)morpholine 3179-63-3 7250-87-5, 1,3-Di-4-morpholinyl-2-propanol **14205-39-1**, Methyl 3-aminocrotonate 15768-07-7, Methyl benzylideneacetoacetate 21829-25-4 39562-37-3, Methyl

3-cyanobenzylideneacetoacetate 67593-46-8, Methyl 2-chlorobenzylideneacetoacetate 70677-78-0 74073-22-6 90961-43-6, Methyl 3-chlorobenzylideneacetoacetate 92565-17-8 92565-18-9, 2-Tetrahydrofuranylmethyl 3-nitrobenzylideneacetoacetate 92565-37-2 102993-41-9, Methyl 3-fluorobenzylideneacetoacetate 103295-95-0, Methyl 3-trifluoromethylbenzylideneacetoacetate 103785-59-7, Methyl 2-bromobenzylideneacetoacetate 130064-42-5, 2-Tetrahydrofuranylmethyl 3-aminocrotonate 138661-03-7 157558-79-7, Methyl 3-bromobenzylideneacetoacetate 222988-50-3, 5-Oxo-2-tetrahydrofuranylmethyl 2-nitrobenzylideneacetoacetate 222988-51-4, Methyl 4-chloro-3-nitrobenzylideneacetoacetate 222988-52-5, Methyl 3-acetylaminobenzylideneacetoacetate 222988-53-6, Methyl 3-hydroxybenzylideneacetoacetate 223136-50-3 223136-52-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cardioprotectant pyridine double esters)

L9 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:429071 CAPLUS
DOCUMENT NUMBER: 115:29071
TITLE: Synthesis of carbon-11 labeled calcium channel antagonists
AUTHOR(S): Holschbach, M.; Roden, W.; Hamkens, W.
CORPORATE SOURCE: Inst. Med., Res. Cent. Juelich, Juelich, D-5170, Germany
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1991), 29(4), 431-42
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:29071
GI



I

AB Dihydropyridines I [R = Me-11C; R1 = Me, R2 = 2-NO2, 2-CF3; R1 = Me2CHCH2, R2 = 2-NO2; R1 = Et, R2 = 3-NO2] were prepared by a modified Hantzsch cyclocondensation of R2C6H4CHO, MeC(NH2):CHCO2R1, and MeS(O)2CH2CH2O2CCH2COMe to give 41-76% I [R = MeS(O)2CH2CH2] and sequential protective group cleavage and alkylation of the corresponding monocarboxylic acid salt with MeI-11C.

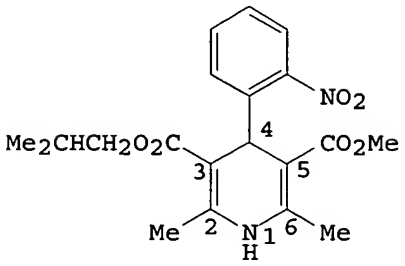
IT 7318-00-5, Ethyl 3-aminocrotonate **14205-39-1**, Methyl 3-aminocrotonate 52937-90-3, Isobutyl 3-aminocrotonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(Hantzsch cyclocondensation of, with aromatic aldehydes and (methylsulfonyl)ethyl acetoacetate)

IT 123973-73-9P **134430-62-9P** 134430-63-0P 134430-64-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L9 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:138871 CAPLUS
DOCUMENT NUMBER: 112:138871

10/520,066

TITLE: Syntheses of [4-carbon-14]- and [6-carbon-14]nisoldipine
AUTHOR(S): Scherling, D.; Pleiss, U.
CORPORATE SOURCE: Inst. Pharmacokinet., Bayer A.-G., Wuppertal, D-5600, Fed. Rep. Ger.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(12), 1393-400
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:138871
GI



I

AB The synthesis of [4-14C]nisoldipine I starting from di-Me [14C]formamide (II) was described. II reacts with 2-O2NC6H4Li yielding 2-nitro[7-14C]benzaldehyde which on Knoevenagel condensation with iso-Bu acetoacetate yielded iso-Bu 2-(2-nitro[7-14C]benzylidene)acetoacetate (III). Key reaction step was the cyclizing Michael addition III with Me 3-aminocrotonate to give I.

IT **14205-39-1**, Methyl 3-aminocrotonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with carbon-14 labeled iso-Bu nitrobenzylideneacetylacetate)

IT **117131-06-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with iso-Bu nitrobenzylideneacetylacetate)

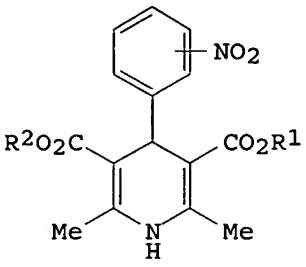
IT **125945-92-8P 125970-62-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L9 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:8051 CAPLUS
DOCUMENT NUMBER: 110:8051
TITLE: Preparation of 4-aryl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylates as antiangina and antihypertensive agents
INVENTOR(S): Cupka, Pavol; Rybar, Alfonz; Svobodova, Xenia; Mahrla, Zdeno; Zlatinsky, Emil; Simko, Marian; Nevydal, Josef; Kosalko, Rudolf; Martvon, Augustin
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 4 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Slovak
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 243591	B1	19860612	CS 1985-526	19850125

PRIORITY APPLN. INFO.: CS 1985-526 19850125

GI



I

AB The title compds. (I) (R1, R2 = straight or branched C1-5 alkyl, optionally interrupted with O) are prepared by reaction of MeCOCH2CO2R1 (II), (O2N)C6H4CH(O2CMe)2 (III), and MeC(NH2):CHCOR2 (IV) in an inert organic solvent at 20-150°. I are antiangina and antihypersensitive agents (no data). A mixture of 2-(O2N)C6H4CH(O2CMe)2 7.54 g, II (R1 = Me) 4 mL, IV (R2 = Me) 4.1 g, and MeOH 10 mL was refluxed 7 h, cooled, and filtered to obtain a crude product which was recrystd. from EtOAc to give 65% I (R1, R2 = Me; NO2 in 2-position).

IT **14205-39-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with Me acetoacetate and nitrobenzaldehyde diacetate)

IT 21829-09-4P 21829-10-7P 21829-25-4P 21829-26-5P 21829-27-6P
21829-28-7P 21881-54-9P 21881-77-6P 21881-78-7P 22609-70-7P
22609-71-8P 22609-72-9P 22609-73-0P 39562-18-0P 39562-70-4P
63675-72-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiangina and antihypertensive agent)

L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:55851 CAPLUS
DOCUMENT NUMBER: 108:55851
TITLE: Crystal structures and pharmacologic activities of 1,4-dihydropyridine calcium channel antagonists of the isobutyl methyl 2,6-dimethyl-4-(substituted phenyl)-1,4-dihydropyridine-3,5-dicarboxylate (nisoldipine) series
AUTHOR(S): Fossheim, R.; Joslyn, A.; Solo, A. J.; Luchowski, E.; Rutledge, A.; Triggle, D. J.
CORPORATE SOURCE: Dep. Chem., Univ. Oslo, Oslo, 0315, Norway
SOURCE: Journal of Medicinal Chemistry (1988), 31(2), 300-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:55851

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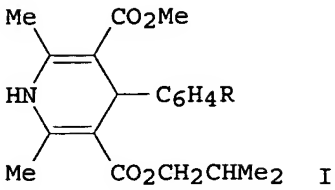


I

AB Nine racemic iso-Bu Me 2,6-dimethyl-4-aryl-1,4-dihydropyridine-3,5-dicarboxylates (I; R = H, 2-NO2, 3-NO2, 3-cyano, 3-OMe, 4-F, 2-CF3, 3-CF3, 4-Cl) including nisoldipine (R = 2-NO2) were prepared and evaluated as Ca channel antagonists against binding of nitrendipine tritiated in the methoxy group and K+-depolarization-induced tension responses in intestinal smooth muscle. The x-ray crystal structures of I (R = H, 2-NO2, 3-NO2, 3-cyano, 3-OMe, 4-F) were determined The degree of 1,4-dihydropyridine ring puckering depends on the nature and position of the Ph substituent and the inter-ring conformation. Different ester substituents affect the ring puckering to a small extent in most cases. Pharmacol. and radioligand binding activities for the 9 compds. studied show a parallel dependence on the Ph substituent, but the compds. are .apprx.10 times more active in the radioligand binding assay than in the pharmacol. assay. Pharmacol. activity increases with increasing dihydropyridine ring planarity.

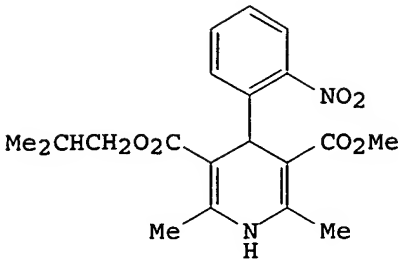
IT **14205-39-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Hantzsch reaction of, with iso-Bu acetoacetate and (trifluoromethyl)benzaldehydes, dihydropyridines from)

IT **63675-72-9P**, (±)-Nisoldipine 111556-83-3P 111556-84-4P 111556-85-5P 111556-86-6P 113578-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, mol. structure, calcium channel antagonistic activity, and nitrendipine binding inhibition of)

L9 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:4897 CAPLUS
DOCUMENT NUMBER: 106:4897
TITLE: Isobutyl 2,6-dimethyl-3-methoxycarbonyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate
INVENTOR(S): Sune Coma, Nuria
PATENT ASSIGNEE(S): Spain
SOURCE: Span., 9 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 546784	A1	19860101	ES 1985-546784	19850909

PRIORITY APPLN. INFO.: ES 1985-546784 19850909
GI



I

AB Title compound I was prepared as follows. A mixture of 2-O2NC6H4CH(OAc)2, Me2CHCH2O2CCH2COMe, and Me(H2N)C:CHCO2Me in EtOH-pyridine was refluxed for 7 h to give 58% I.

IT **14205-39-1**, Methyl 3-aminocrotonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with acetoacetate and nitrobenzaldehyde diacetate)

IT **63675-72-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by cyclocondensation of acetoacetate, aminocrotonate, and nitrobenzaldehyde diacetate)

L9 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:156503 CAPLUS
DOCUMENT NUMBER: 100:156503
TITLE: Use of 1,4-dihydropyridines as antiarteriosclerotics
INVENTOR(S): Seuter, Friedel; Bossert, Friedrich; Meyer, Horst; Wehinger, Egbert; Boeshagen, Horst
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3222367	A1	19831215	DE 1982-3222367	19820615
DE 3222367	C2	19920213		
JP 59005114	A2	19840112	JP 1983-103003	19830610
JP 05053774	B4	19930810		
BE 897035	A1	19831213	BE 1983-210988	19830613
CA 1228549	A1	19871027	CA 1983-430227	19830613
FR 2528425	A1	19831216	FR 1983-9798	19830614
FR 2528425	B1	19870206		
ES 523244	A1	19840316	ES 1983-523244	19830614
ZA 8304344	A	19840328	ZA 1983-4344	19830614

PRIORITY APPLN. INFO.: DE 1982-3222367 A 19820615
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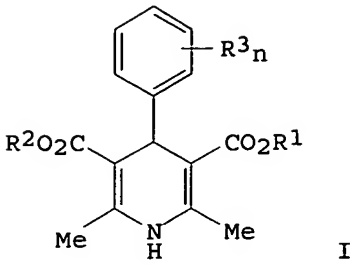

I

AB Dihydropyridines I [R1, R2 = C1-12 alkyl or alkoxyalkyl, alkyl (un)substituted with Cl or F; R3 = NO2, CF3, halo, cyano; n = 1,2], useful as antiatherosclerotics or in treating arterioslcerosis, were prepared Boiling 3-O2NC6H4CH:C(CO2Et)COMe and H2NCMe:CHCO2Me in EtOH 10 h gave 67% I (R1 = Me, R2 = Et, R3n = 3-NO2), which reduced arteriosclerotic plaque in rat arteries by 49% at 30 mg/kg orally.

IT **14205-39-1** 52937-92-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with Et (nitrobenzylidene)acetoacetate, dihydropyridinedicarboxylate by)

IT 22609-73-0P **63675-72-9P** 88284-22-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiarteriosclerotic)

L9 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:484831 CAPLUS
DOCUMENT NUMBER: 87:84831
TITLE: Isobutyl 2,6-dimethyl-3-methoxycarbonyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate with coronary therapeutic action
INVENTOR(S): Wehinger, Egbert; Bossert, Friedrich; Heise, Arend; Kazda, Stanislav; Stoepel, Kurt; Vater, Wulf
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2549568	A1	19770518	DE 1975-2549568	19751105
DE 2549568	B2	19800821		
DE 2549568	C3	19811029		
NO 7603608	A	19770506	NO 1976-3608	19761022
NO 145574	B	19820111		
NO 145574	C	19820421		
JP 52059161	A2	19770516	JP 1976-129540	19761029
JP 56047185	B4	19811107		
IL 50817	A1	19790725	IL 1976-50817	19761102
CS 200499	P	19800915	CS 1976-7068	19761102
CH 623038	A	19810515	CH 1976-13819	19761102
RO 70295	P	19810817	RO 1976-88294	19761102
FI 7603160	A	19770506	FI 1976-3160	19761103
FI 60704	B	19811130		
FI 60704	C	19820310		
NL 7612198	A	19770509	NL 1976-12198	19761103
NL 175915	B	19840816		
NL 175915	C	19850116		

AT 352129	B	19790910	AT 1976-8142		19761103
AT 7608142	A	19790215			
PL 106084	P	19791130	PL 1976-193438		19761103
PL 105940	P	19791130	PL 1976-201800		19761103
BE 847968	A1	19770504	BE 1976-172063		19761104
DK 7604984	A	19770506	DK 1976-4984		19761104
DK 146762	B	19831227			
DK 146762	C	19840612			
SE 7612308	A	19770506	SE 1976-12308		19761104
SE 423542	B	19820510			
SE 423542	C	19820819			
ZA 7606622	A	19771026	ZA 1976-6622		19761104
CA 1085406	A1	19800909	CA 1976-264921		19761104
FR 2330395	A1	19770603	FR 1976-33488		19761105
FR 2330395	B1	19781222			
AU 498964	B2	19790329	AU 1976-19358		19761105
AU 7619358	A1	19780511			
CS 200500	P	19800915	CS 1977-6535		19771007
US 4154839	A	19790515	US 1978-903573		19780508
CH 622779	A	19810430	CH 1980-5678		19800724
PRIORITY APPLN. INFO.:			DE 1975-2549568	A	19751105
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			CS 1976-7068		19761102
			US 1976-738383	A1	19761102

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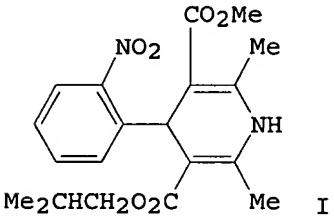

I

AB The title compound (I) was prepared in 78% yield by treating 2-O2NC6H4CH:C(COMe)CO2CH2CHMe2 with H2NCMe:CHCO2Me. At 0.003 mg/kg sublingually in dogs I increased the myocardial blood flow by 23% with a halflife of 100 min.

IT **14205-39-1** 52937-90-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with nitrobenzylideneacetoacetate)

IT **63675-72-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cardiac activity of)

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FILE 'USPAT2' ENTERED AT 09:49:59 ON 13 DEC 2005

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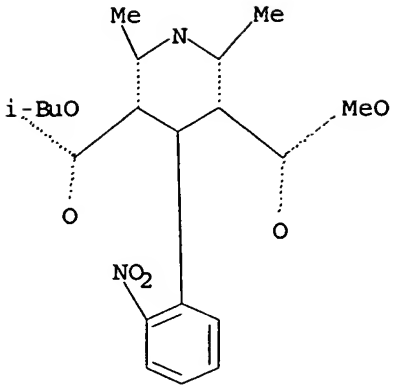
L4 STR



Structure attributes must be viewed using STN Express query preparation.
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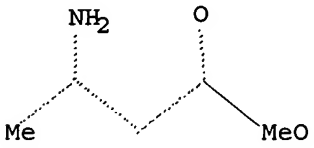

Structure attributes must be viewed using STN Express query preparation.
L6 21 SEA FILE=REGISTRY SSS FUL L4
L7 315 SEA FILE=REGISTRY SSS FUL L5
L10 3 SEA L6 AND L7

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L10 ANSWER 1 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2005:275457 USPATFULL
TITLE: Industrial process for the synthesis of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (nisoldipine)
INVENTOR(S): Ferrari, Massimo, Cenate Sotto, ITALY
Ghezzi, Marcello, Curno, ITALY
Alberelli, Manuel, Casazza, ITALY
Ambrosini, Alberto, Lallio, ITALY

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005240022	A1	20051027	
APPLICATION INFO.:	US 2003-520066	A1	20030626	(10)
	WO 2003-EP6755		20030626	
			20050103	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 2003-MI200200144520020701	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GIFFORD, KRASS, GROH, SPRINKLE & CITKOWSKI, P.C, PO BOX 7021, TROY, MI, 48007-7021, US
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 222

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Synthetic process of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)3,5-pyridine dicarboxylate (Nisoldipine) comprising on the reaction of isobutyl 2-(2-nitrobenzylidene)acetoacetate with methyl 3-aminocrotonate in an apolar solvent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 552-89-6, 2-Nitrobenzaldehyde 7779-75-1, Isobutyl acetoacetate
14205-39-1, Methyl 3-aminocrotonate
(synthesis of nisoldipine by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)
IT **63675-72-9P**, Nisoldipine
(synthesis, by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)

=> d l10 2-3 ibib abs hit

L10 ANSWER 2 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2002:304006 USPATFULL
TITLE: Pyridyl compounds and pharmaceutical compositions containing them
INVENTOR(S): Letelier, Carlos Sunkel, Madrid, SPAIN
Munoz, Miguel Fau De Casa-Juana, Madrid, SPAIN
Gomez, Julio Alvarez-Builla, Madrid, SPAIN
Ortega, Jose M. Minguez, Madrid, SPAIN
Statkow, Pierre, Geneva, SWITZERLAND
Straumann, Danielle, Martigny, SWITZERLAND
Chatterjee, Shyam S., Karlsruhe, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Cermol S.A., Evionnaz, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6482841	B1	20021119	
	WO 9919302		19990422	
APPLICATION INFO.:	US 2000-529112		20000407	(9)
	WO 1998-IB1555		19981007	
			20000407	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1997-2364	19971009

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Rotman, Alan L.
ASSISTANT EXAMINER: Desai, Rita
LEGAL REPRESENTATIVE: Young & Thompson
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1042
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

The present invention is concerned with new pyridine double esters of formula (I), their acids, and pharmaceutically acceptable salts. These compounds can be obtained by oxydation of the corresponding 1,4-dihydropyridines, and they are useful as cardioprotective agents in pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 85677-93-6 89267-41-4 **103026-83-1**
(preparation of cardioprotectant pyridine double esters)
IT 100-37-8, Diethylaminoethanol 105-45-3, Methyl acetoacetate 108-01-0, Dimethylaminoethanol 447-61-0, 2-Trifluoromethylbenzaldehyde 622-40-2, 4-(2-Hydroxyethyl)morpholine 3179-63-3 7250-87-5, 1,3-Di-4-morpholinyl-2-propanol **14205-39-1**, Methyl 3-aminocrotonate 15768-07-7, Methyl benzylideneacetoacetate 21829-25-4 39562-37-3, Methyl 3-cyanobenzylideneacetoacetate 67593-46-8, Methyl 2-chlorobenzylideneacetoacetate 70677-78-0 74073-22-6 90961-43-6, Methyl 3-chlorobenzylideneacetoacetate 92565-17-8 92565-18-9, 2-Tetrahydrofuranylmethyl 3-nitrobenzylideneacetoacetate 92565-37-2 102993-41-9, Methyl 3-fluorobenzylideneacetoacetate 103295-95-0, Methyl 3-trifluoromethylbenzylideneacetoacetate 103785-59-7, Methyl 2-bromobenzylideneacetoacetate 130064-42-5, 2-Tetrahydrofuranylmethyl 3-aminocrotonate 138661-03-7 157558-79-7, Methyl 3-bromobenzylideneacetoacetate 222988-50-3, 5-Oxo-2-tetrahydrofuranylmethyl 2-nitrobenzylideneacetoacetate 222988-51-4, Methyl 4-chloro-3-nitrobenzylideneacetoacetate 222988-52-5, Methyl 3-acetylaminobenzylideneacetoacetate 222988-53-6, Methyl 3-hydroxybenzylideneacetoacetate 223136-50-3 223136-52-5
(preparation of cardioprotectant pyridine double esters)

L10 ANSWER 3 OF 3 USPATFULL on STN
ACCESSION NUMBER: 79:24268 USPATFULL
TITLE: 2,6-Dimethyl-3-carboxymethoxy-4-(2-nitrophenyl)-5-carbisobutoxy-1,4-dihydropyridine
INVENTOR(S): Wehinger, Egbert, Velbert, Germany, Federal Republic of
Bossert, Friedrich, Wuppertal, Germany, Federal Republic of
Heise, Arend, Wuppertal, Germany, Federal Republic of
Kazda, Stanislav, Wuppertal, Germany, Federal Republic of
Stoepel, Kurt, Wuppertal, Germany, Federal Republic of
Vater, Wulf, Leverkusen, Germany, Federal Republic of
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4154839		19790515
APPLICATION INFO.:	US 1978-903573		19780508 (5)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1976-738383, filed on 2 Nov 1976, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1975-2549568	19751105

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Jacobs & Jacobs
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 246
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate demonstrates the unique ability of increasing myocardial perfusion upon oral or intravenous administration. Methods of preparing the compound, its use in coronary conditions and pharmaceutical compositions for effecting that use are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

10/520,066

IT **14205-39-1** 52937-90-3
(condensation of, with nitrobenzylideneacetoacetate)
IT **63675-72-9P**
(preparation and cardiac activity of)

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